AKI Clinical Trials

AKI Workshop Ras El Bar
8-10 February 2015

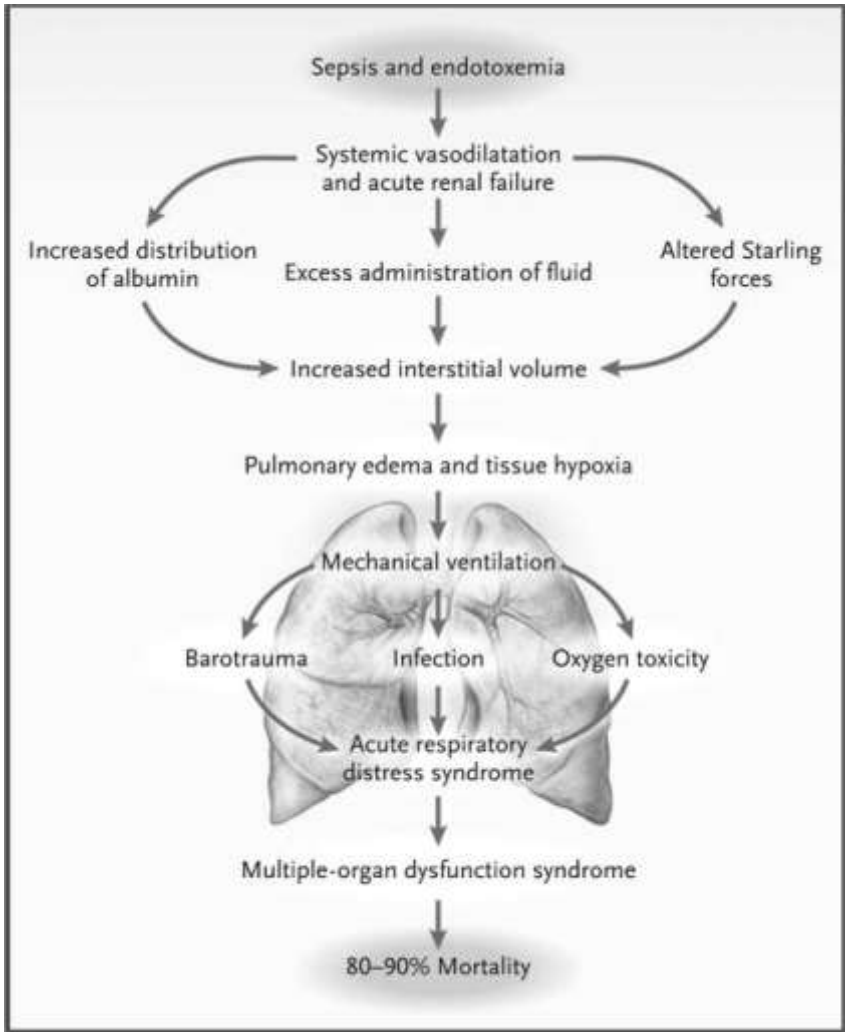
Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

Key clinical trials

- Fluid therapy – what kind and how much?
- RRT – when, what and how much?
- Cardiac surgery – off pump or on pump
- Cardio-Renal failure and contrast nephropathy
- Systems management and AKI

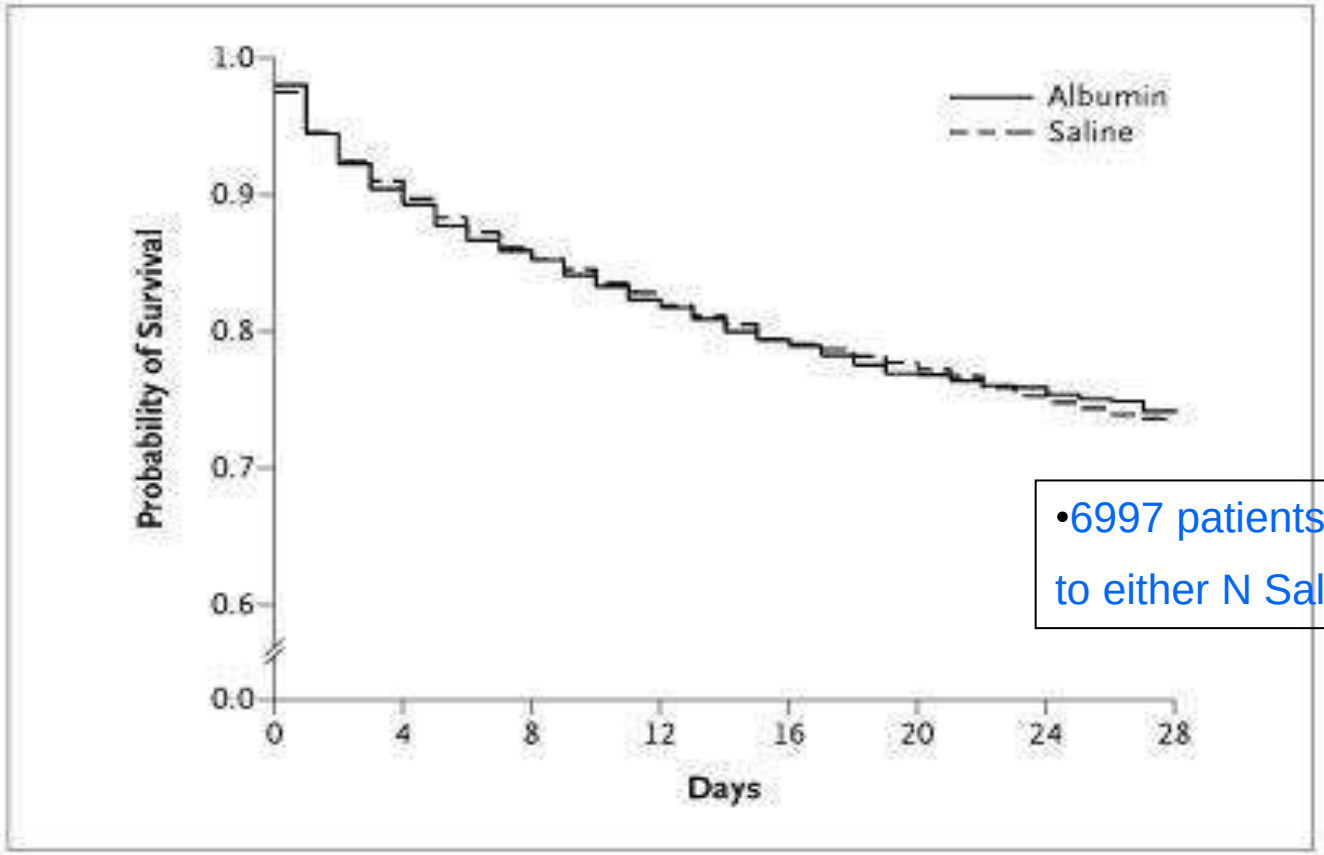
Events in sepsis and endotoxemia leading to pulmonary edema, hypoxia, mechanical ventilation, ARDS, and high mortality.



Schrier R W CJASN 2010;5:733-739

Crystalloid or Colloid?

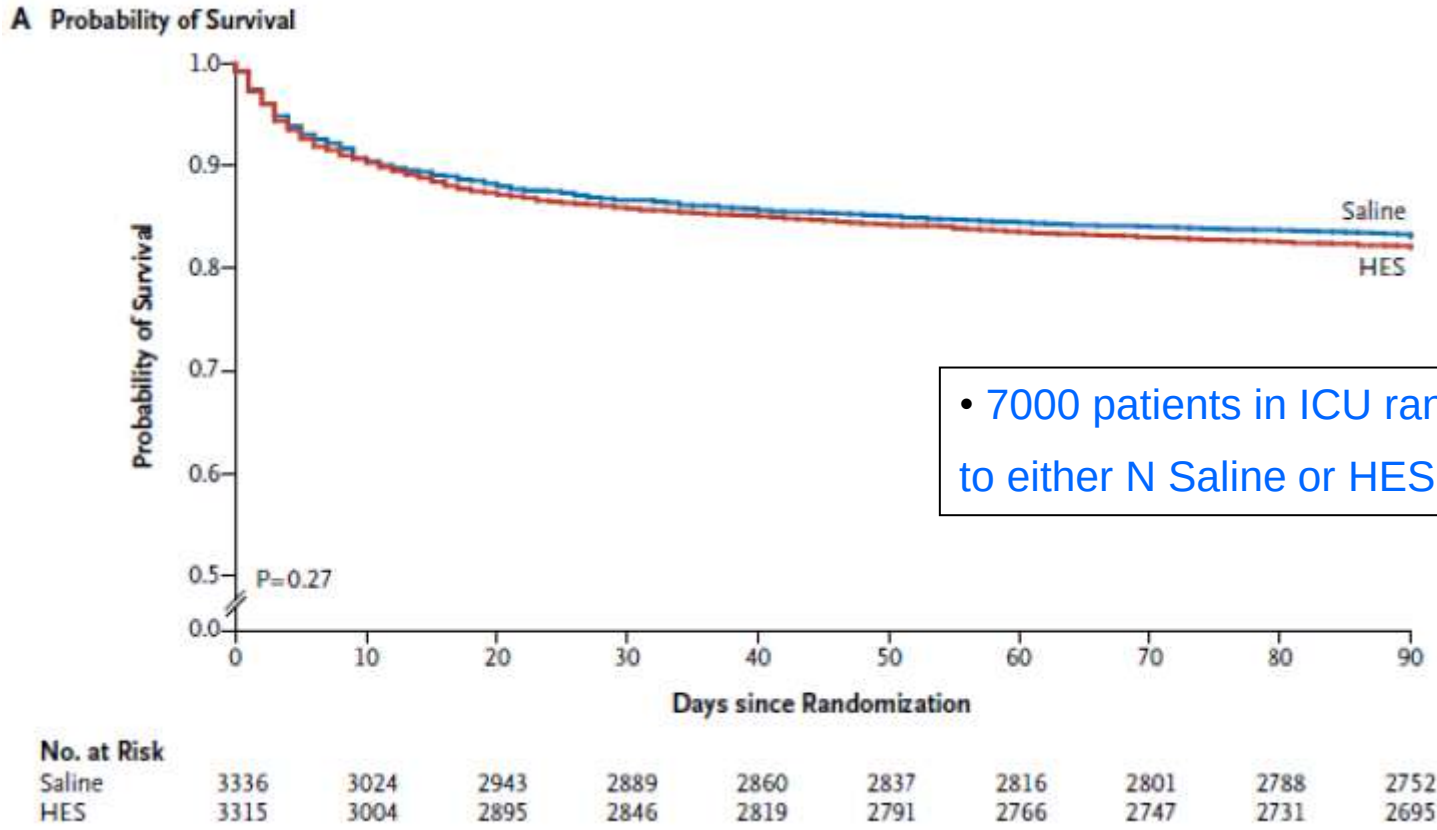
Albumin vs Saline for fluid replacement in ICU – SAFE study



- 6997 patients in ICU randomised to either N Saline or Albumin

The SAFE Study Investigators. N Engl J Med 2004;350:2247-2256.

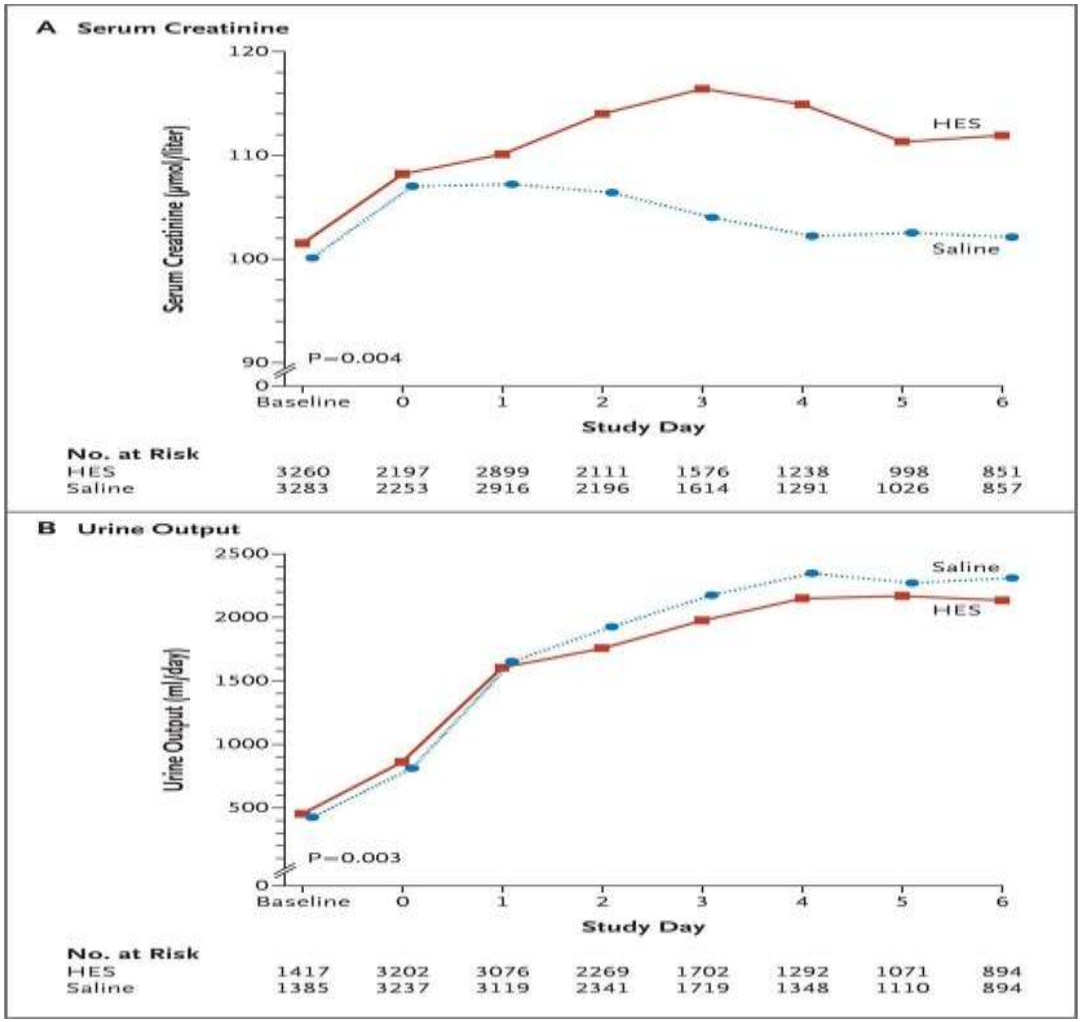
Crystalloid vs Hydroxyethyl Starch – The CHEST study



- 7000 patients in ICU randomised to either N Saline or HES

Myburgh JA et al. N Engl J Med 2012. DOI: 10.1056/NEJMoa1209759

Crystalloid vs Hydroxyethyl Starch – The CHEST study

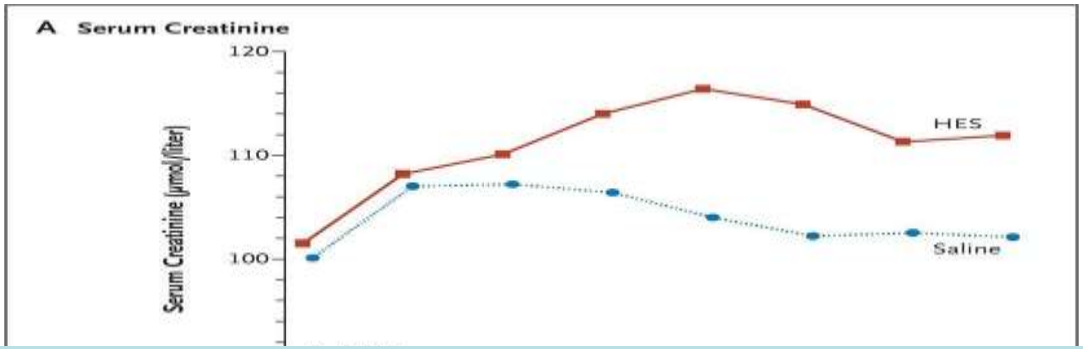


- 7000 patients in ICU randomised

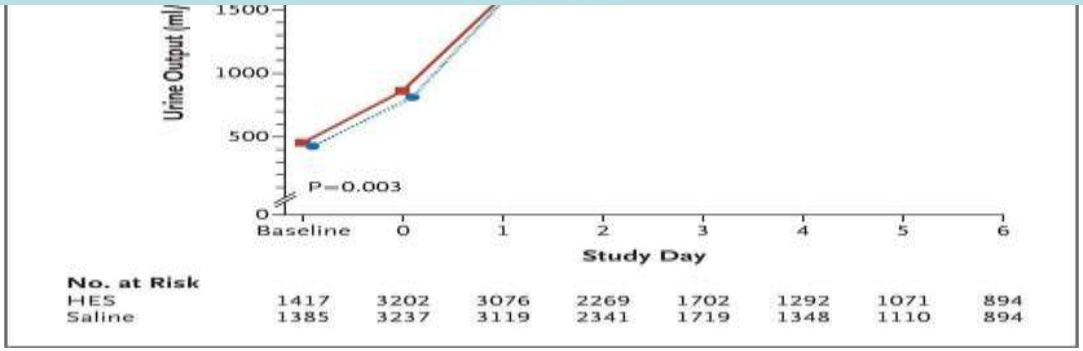
to either N Saline or HES

Myburgh JA et al. N Engl J Med 2012. DOI: 10.1056/NEJMoa1209759

Crystalloid vs Hydroxyethyl Starch – The CHEST study



Saline/Crystalloid is the optimal fluid replacement

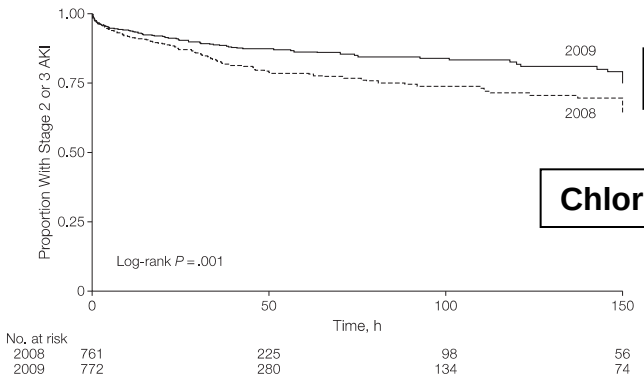


Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

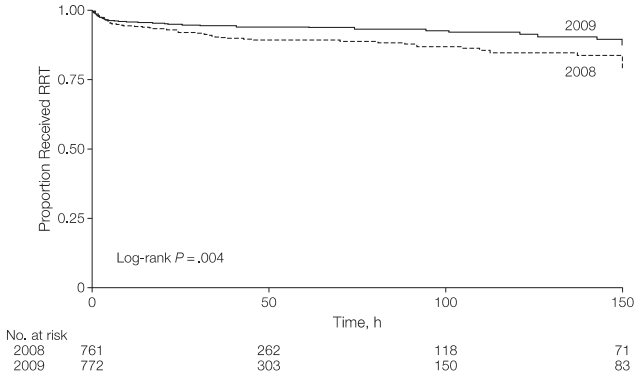
Chloride-Rich vs Chloride poor fluid

Figure 1. Development of Stage 2 or 3 Acute Kidney Injury (AKI) While in the Intensive Care Unit (ICU)



Stage 2 or 3 defined according to the Kidney Disease: Improving Global Outcomes clinical practice guideline.

Figure 2. Renal Replacement Therapy (RRT) in the Intensive Care Unit (ICU)



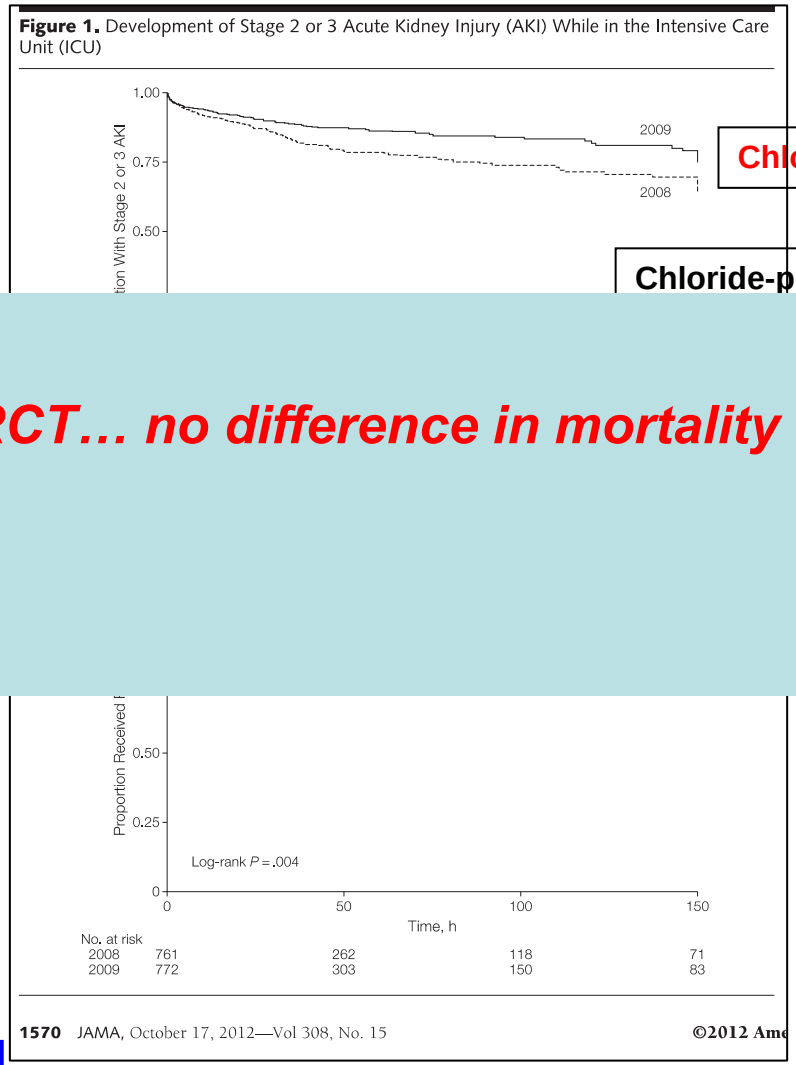
Chloride-rich fluid – N saline

Chloride-poor fluid – Hartmanns, chloride-poor albumin

- Open label sequential pilot of 760 patients on ICU

Yunos M et al Volume 308(15), 17 October 2012, p 1566–1572

Chloride-Rich vs Chloride poor fluid



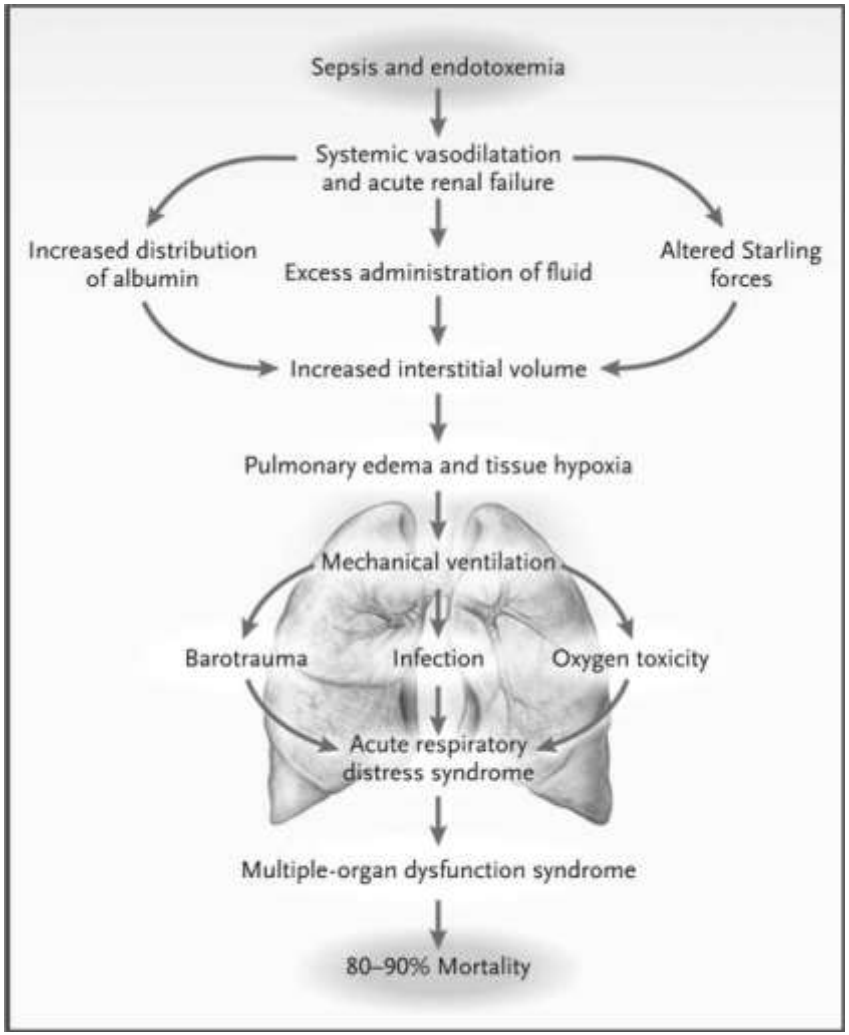
Chloride-rich fluid – N saline

Chloride-poor fluid – Hartmanns, chloride-poor albumin

Not an RCT… no difference in mortality or RRT on hospital discharge

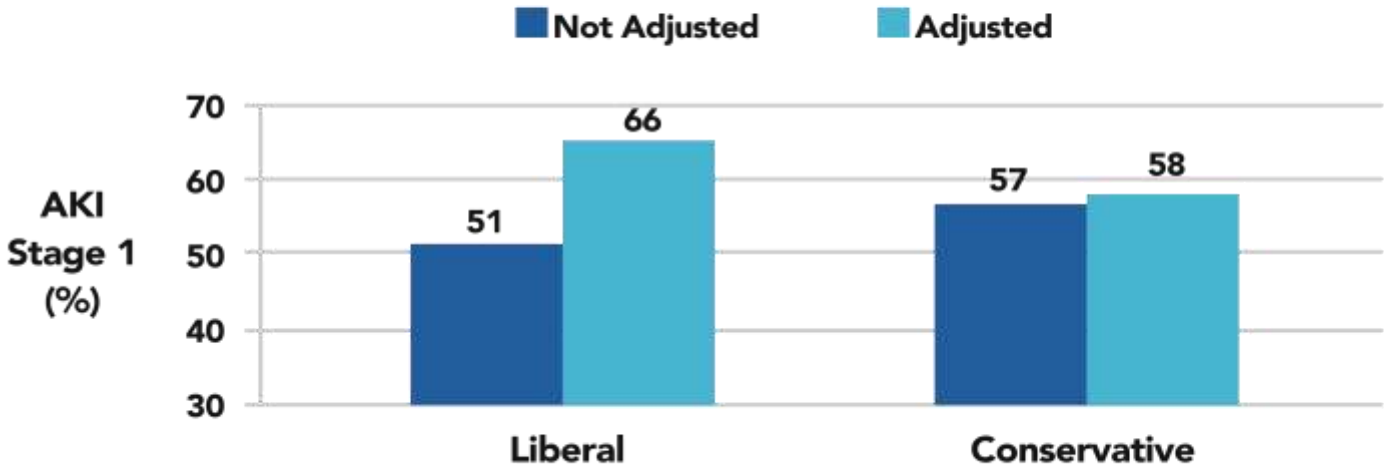
Yunos M et al Volume 308(15), 17 October 2012, p 1566–1572

Events in sepsis and endotoxemia leading to pulmonary edema, hypoxia, mechanical ventilation, ARDS, and high mortality.



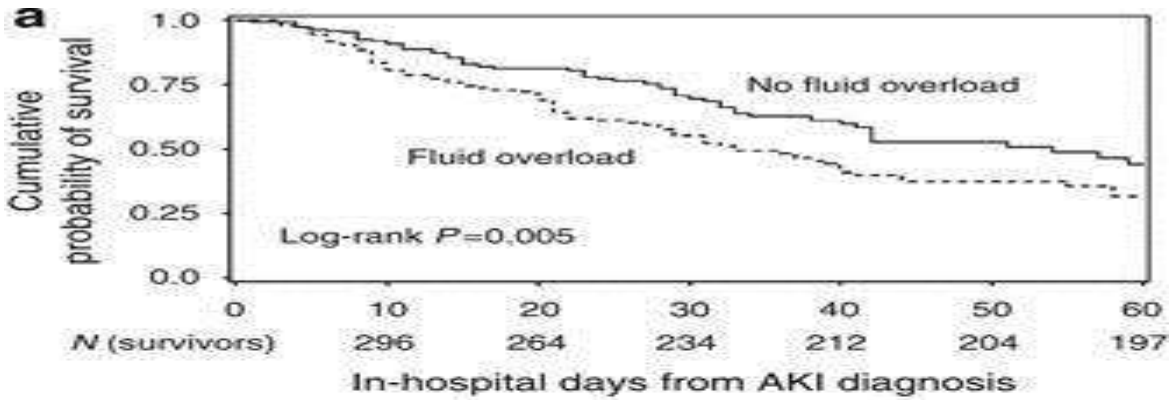
Schrier R W CJASN 2010;5:733-739

Figure 3. Incidence of AKI stage 1 in patients with acute respiratory distress syndrome randomized to different fluid management strategies.

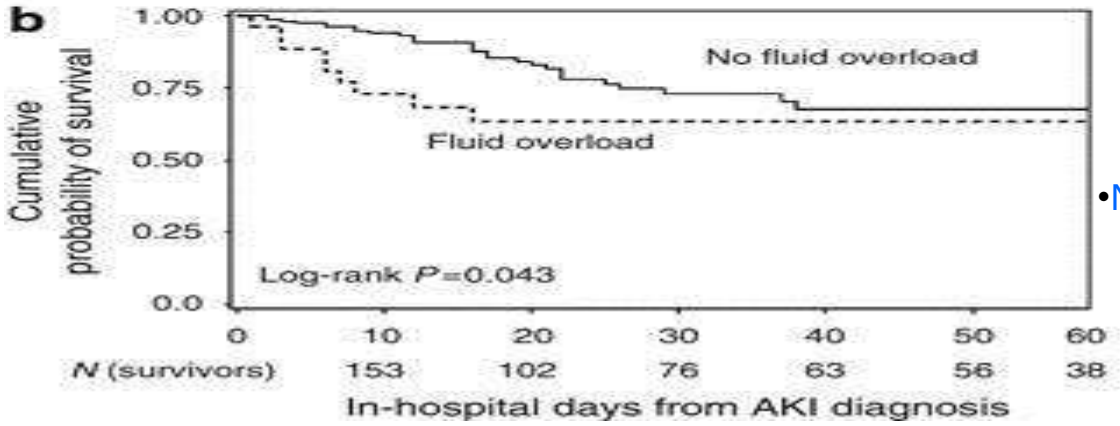


Reprinted with permission from reference 31.

Fluid Accumulation and survival in AKI in ICU



•Dialysis Patients



•Non-Dialysis Patients

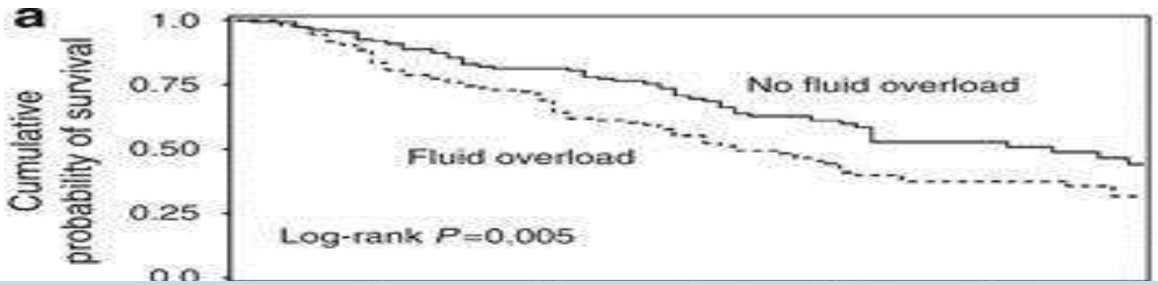
Prospective, Observational Study.
PICARD study group

•618 patients.

•Fluid overload had no impact on renal survival

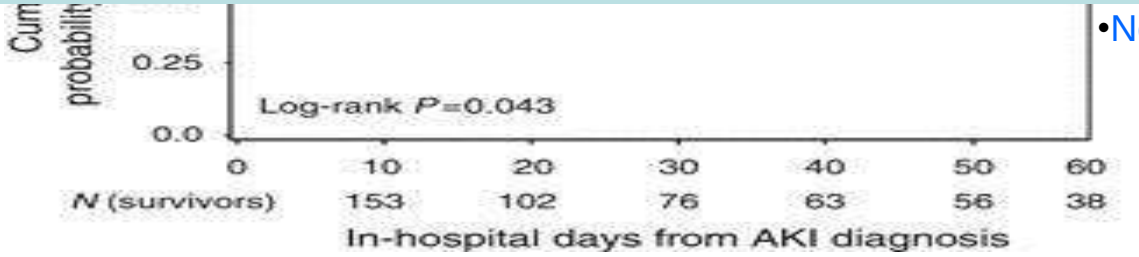
Bouchard J et al. *Kidney International* (2009) 76, 422–427;

Fluid Accumulation and survival in AKI in ICU



•Dialysis Patients

Fluid accumulation association with adverse outcomes



•Non-Dialysis Patients

Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

Key clinical trials

-
- Fluid therapy – what kind and how much?
- RRT – when, what and how much?
- Cardiac surgery – off pump or on pump
- Cardio-Renal failure and contrast nephropathy
- Systems management and AKI

When to start RRT?

Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

When to start RRT

***Panel 2:* Conventional criteria for initiation of renal replacement therapy in acute kidney injury**

1. Anuria (negligible urine output for 6 h)
2. Severe oliguria (urine output <200 mL over 12 h)
3. Hyperkalaemia (potassium concentration >6·5 mmol/L)
4. Severe metabolic acidosis (pH <7·2 despite normal or low partial pressure of carbon dioxide in arterial blood)
5. Volume overload (especially pulmonary oedema unresponsive to diuretics)
6. Pronounced azotaemia (urea concentrations >30 mmol/L or creatinine concentrations >300 µmol/L)
7. Clinical complications of uraemia (eg, encephalopathy, pericarditis, neuropathy)*

*Complications of uraemia should be prevented by avoidance of unnecessarily high degrees of azotaemia.

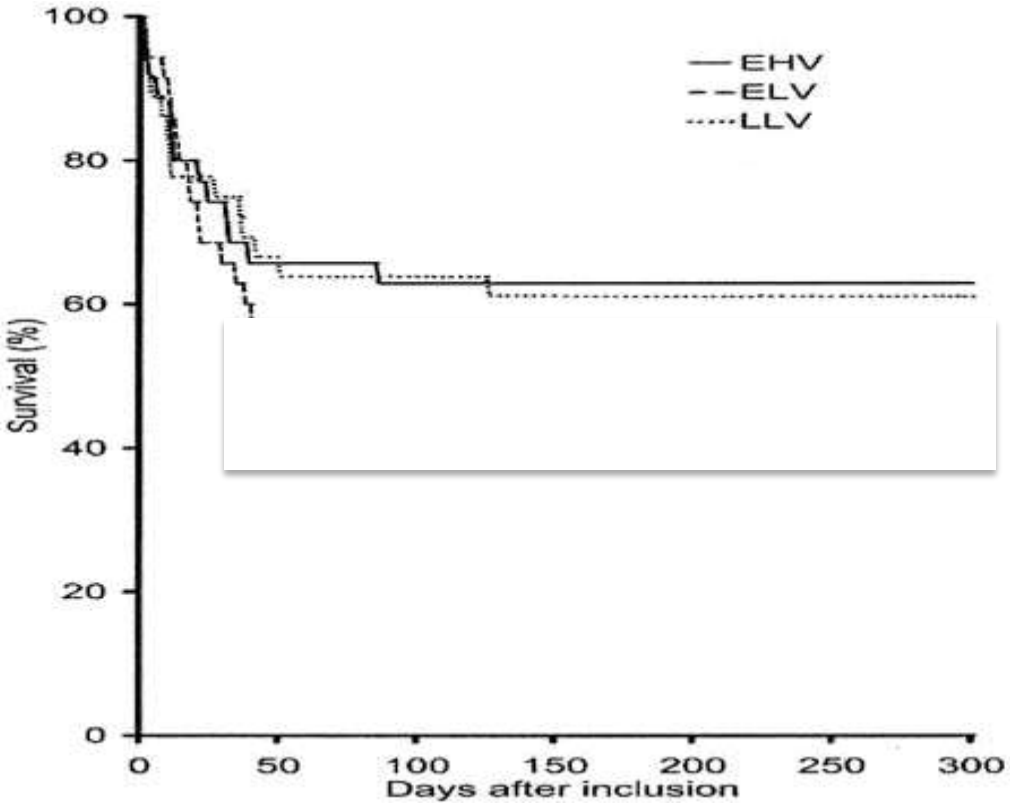
Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

AKI – Early versus Late start

-
- Only 2 RCTs! – 106 patients and 28 patients
- Mostly observational studies with varying criteria to start
- Observational studies tend to favour early start

Early vs late RRT post cardiac surgery



- **RCT of 106 patients post cardiac surgery**
- **Early start: Oliguria for > 6 hours despite optimum fluid state with creat clearance< 20 mls**
- **Late Start: Urea>40, K>6.5 severe pulmonary oedema**

Effects of early high-volume continuous venovenous hemofiltration on survival and recovery of renal function in intensive care patients with acute renal failure: A prospective, randomized trial. Bouman, Catherine Critical Care Medicine. 30(10):2205-2211, October 2002.

Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

Early vs late RRT post cardiac surgery

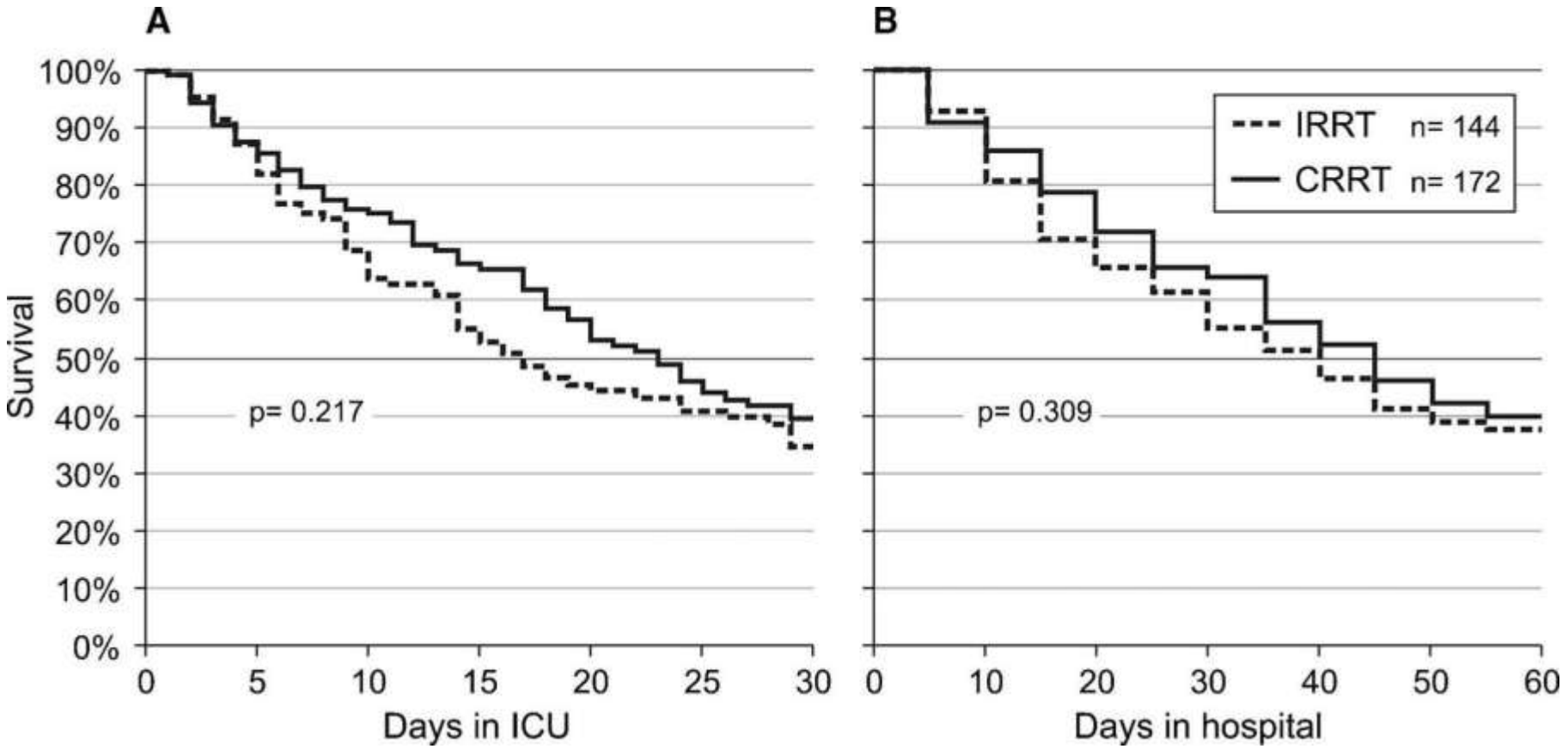
- **RCT of 106 patients post cardiac surgery**
- **Early start: Oliguria for > 6 hours**

- **No difference between early and late start**
- ***But this is a small study***

Key clinical trials

-
- Fluid therapy – what kind and how much?
- RRT – when, what and how much?
- Cardiac surgery – off pump or on pump
- Cardio-Renal failure and contrast nephropathy
- Systems management and AKI

Intermittent (IRRT) or continuous (CRRT) renal replacement therapy on mortality



Lins R L et al. Nephrol. Dial. Transplant. 2009;24:512-518

Randomized trials comparing CRRT with IHD in ICU

Table 1 | Randomized trials comparing CRRT with IHD in the ICU

Study	Type	*n*	Comparison	Mortality*	Renal recovery‡	Comment
Lins *et al.* (2009)[30]	Multicenter RCT	316	CVVHF vs IHD	58% vs 63% (*P*=ns)	35% vs 29% (*P*=ns)	Some hemodynamically unstable patients excluded
Vinsonneau *et al.* (2006)[29]	Multicenter RCT	359	CVVHDF vs IHD	32% vs 33% at day 60 (*P*=ns)	63% vs 60% (*P*=ns)	Change in relative survival during time-course of study
Uehlinger *et al.* (2005)[28]	Single-center RCT	125	CVVHDF vs IHD	47% vs 51% (*P*=ns)	50% vs 42% (*P*=ns)	Study terminated early
Augustine *et al.* (2004)[27]	Single-center RCT	80	CVVHD vs IHD	68% vs 70% (*P*=ns)	13% vs 10% (*P*=ns)	—
Kielstein *et al.* (2004)[26]	Single-center RCT	39	CVVHF vs extended daily dialysis	40% vs 40% (*P*=ns)	Not reported	Survival was not the primary outcome
Mehta *et al.* (2001)[24]	Multicenter RCT	166	CVVHDF vs IHD	66% vs 48% (*P*=0.02)	30% vs 48% (*P*=ns)	Unbalanced randomization favoring IHD
John *et al.* (2001)[25]	Single-center RCT	30	CVVHF vs IHD	70% vs 70% (*P*=ns)	Not reported	Survival was not the primary outcome

Only prospective randomized controlled trials published in peer-reviewed journals in English are included. *In-hospital mortality unless stated otherwise. ‡Percentage alive and off renal replacement therapy at hospital discharge. Abbreviations: CVVHD, continuous venovenous hemodialysis; CVVHDF, continuous venovenous hemodiafiltration; CVVHF, continuous venovenous hemofiltration; IHD, intermittent hemodialysis; ns, nonsignificant (*P*>0.05); RCT, randomized controlled trial.

Prowle, J. R. & Bellomo, R. (2010) *Nat. Rev. Nephrol.* doi:10.1038/nrneph.2010.100

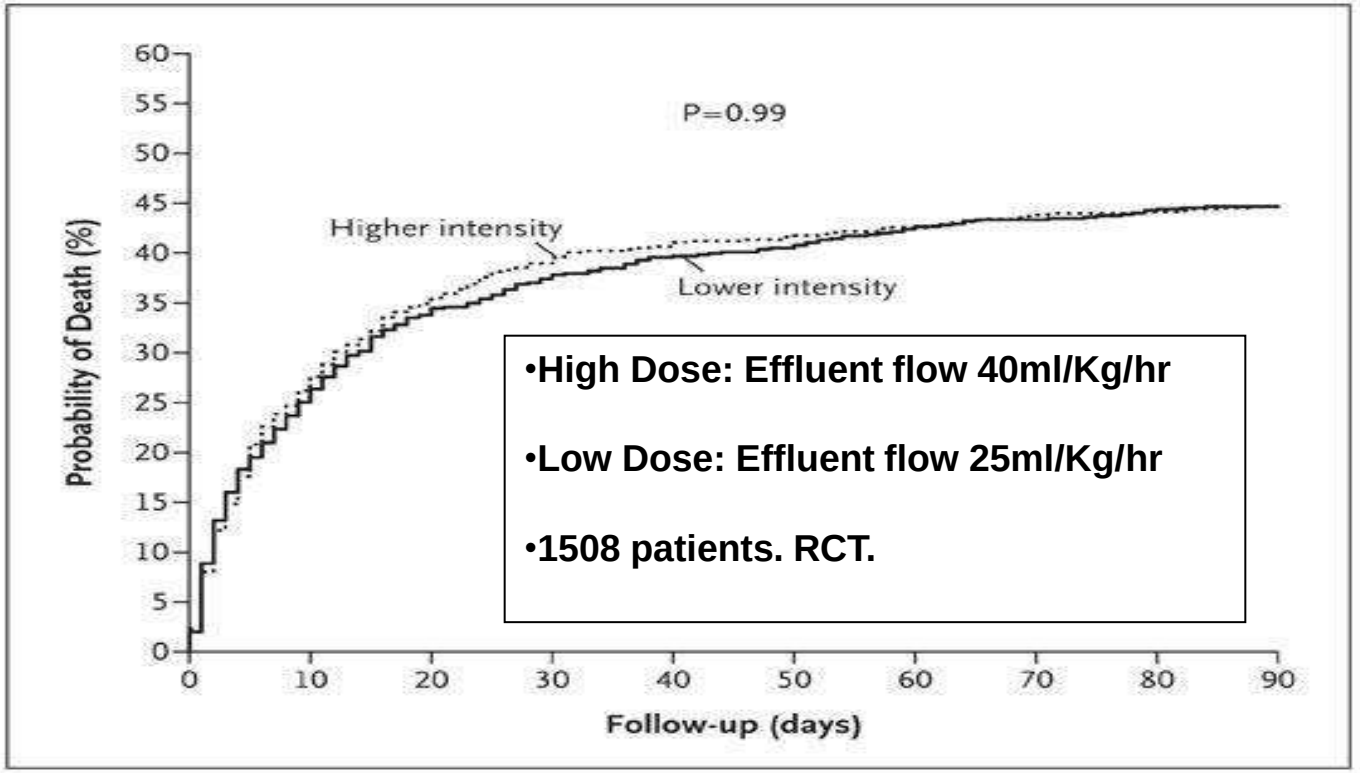
Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

Key clinical trials

-
- Fluid therapy – what kind and how much?
- RRT – when, what and how much?
- Cardiac surgery – off pump or on pump
- Cardio-Renal failure and contrast nephropathy
- Systems management and AKI

Renal study
High vs Low intensity renal replacement

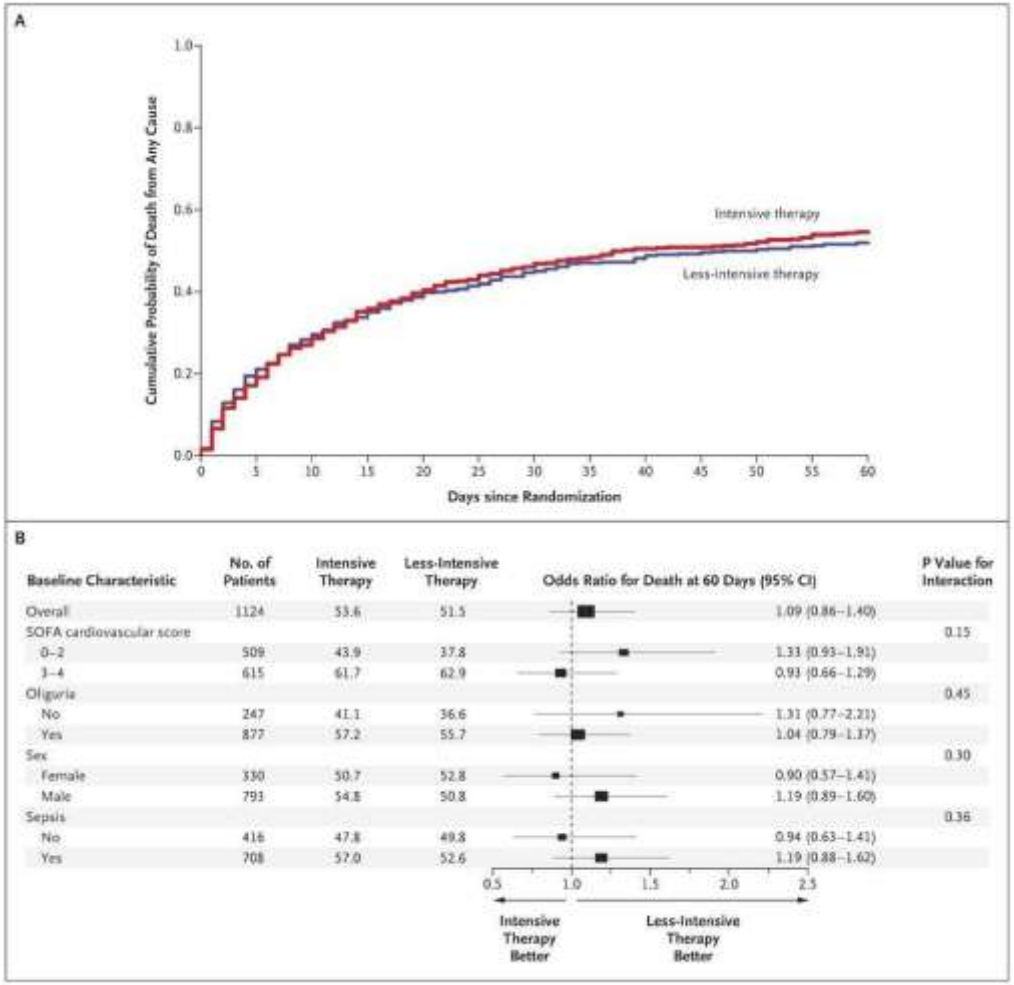


The RENAL Replacement Therapy Study Investigators. N Engl J Med 2009;361:1627-1638.

Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

ATN study – high vs low intensity renal replacement



- **High Dose: Effluent flow 35ml/Kg/hr or 6X week SLED/IHD**
- **Low Dose: Effluent flow 20ml/Kg/hr or 3x week IHD/SLD**
- **530 patients. RCT.**

The VA/NIH Acute Renal Failure Trial NetworkN Engl J Med 2008; 359:7-20

Randomized trials comparing RRT dose on ICU

Table 2 | Randomized controlled trials comparing CRRT dose in the ICU

Study	Type	*n*	Comparison	Mortality	Mortality end point	Comment
RENAL (2009)[18]	Multicenter RCT	1,508	40 ml/kg per h vs 25 ml/kg per h post-dilution CVVHDF	45% vs 45% (*P*=ns)	Day 90	—
ATN (2008)[17]	Multicenter RCT	1,124	Pre-dilution CVVHDF 35 ml/kg per h or SLEDD 6 times weekly or IHD 6 times weekly vs pre-dilution CVVHDF 20 ml/kg per h or SLEDD 3 times weekly or IHD 3 times weekly	54% vs 52% (*P*=ns)	Day 60	Choice of CRRT/SLEDD vs IHD based on daily cardiovascular SOFA score
Tolwani *et al.* (2008)[58]	Single-center RCT	200	Pre-dilution CVVHDF 20 ml/kg per h vs 35 ml/kg per h	56% vs 49% (*P*=ns)	ICU discharge or day 30	—
Saudan *et al.* (2006)[57]	Single-center RCT	204	CVVHF (1–2.5 l/h) vs CVVHDF (1–2.5 l/h HF+1–1.5 l/h HD)	59% vs 39% (*P*=0.0005)	Day 28	Addition of HD to HF (as HDF) vs HF alone
Bouman *et al.* (2002)[53]	Two-center RCT	106	CVVHF 72–96 l per day early vs 24–36 l per day early vs 24–36 l per day late	26% vs 31% (*P*=ns) vs 25% (*P*=ns)	Day 30	Combined trial of dose and timing (early vs late)
Ronco *et al.* (2000)[56]	Single-center RCT	425	Post-dilution CVVHF 20 ml/kg per h vs 35 ml/kg per h vs 45 ml/kg per h	41% vs 57% vs 58% (*P*<0.002 for 20 ml/kg per h vs 35 ml/kg per h and 45 ml/kg per h and *P*=ns for 35 ml/kg per h vs 45 ml/kg per h)	Day 15	Unorthodox mortality outcome (day 15 post-CRRT)

Only prospective randomized controlled trials published in peer-reviewed journals in English are included. Abbreviations: CRRT, continuous renal replacement therapy; CVVHDF, continuous venovenous hemodiafiltration; CVVHF, continuous venovenous hemofiltration; HD, hemodialysis; HDF, hemodiafiltration; HF, hemofiltration; IHD, intermittent hemodialysis; ns, nonsignificant (*P*>0.05); RCT, randomized controlled trial; SLEDD, slow extended-duration dialysis; SOFA, sequential organ failure assessment.

Prowle, J. R. & Bellomo, R. (2010) *Nat. Rev. Nephrol.* doi:10.1038/nrneph.2010.100

KEY CLINICAL TRIALS

-
- Fluid therapy – what kind and how much?
- RRT – when, what and how much?
- Cardiac surgery – off pump or on pump
- Cardio-Renal failure and contrast nephropathy
- Systems management and AKI

Global Kidney Academy

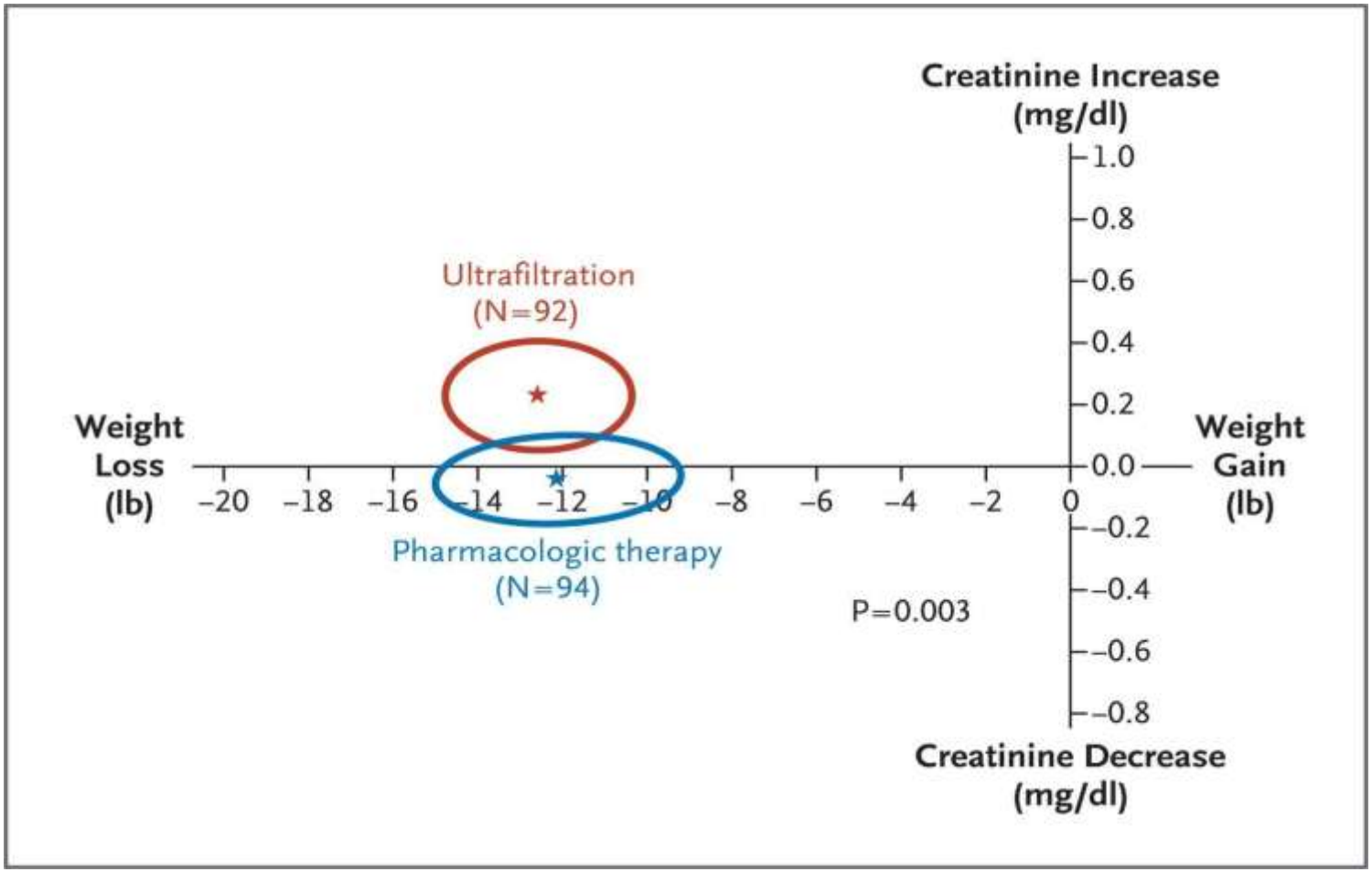
SHEFFIELD KIDNEY INSTITUTE

Ultrafiltration or Diuretics in acute cardiorenal failure – CARESS-HF

- RCT of 188 patients with acute cardio-renal failure
- Randomised to either stepped diuretics or ultrafiltration
- Primary endpoint – change in serum creatinine and weight

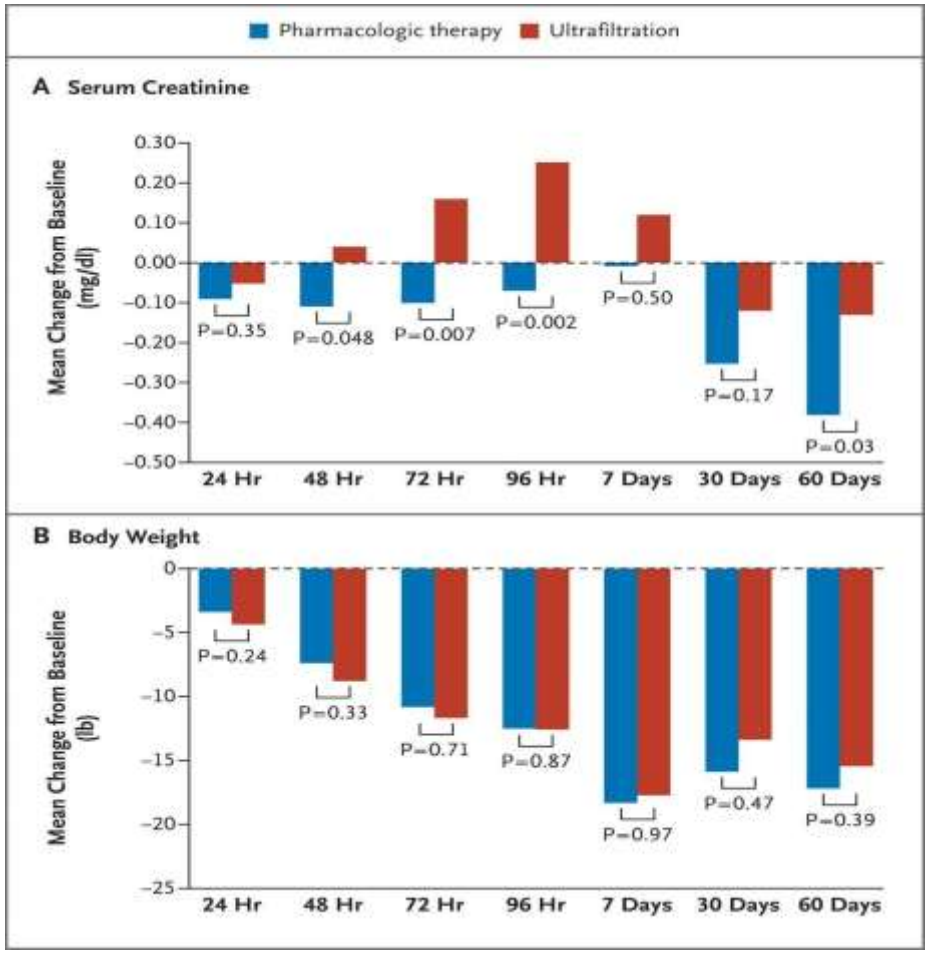
Bart BA et al. N Engl J Med 2012. DOI: 10.1056/NEJMoa1210357

Ultrafiltration or Diuretics in acute cardiorenal failure – CARESS_HF



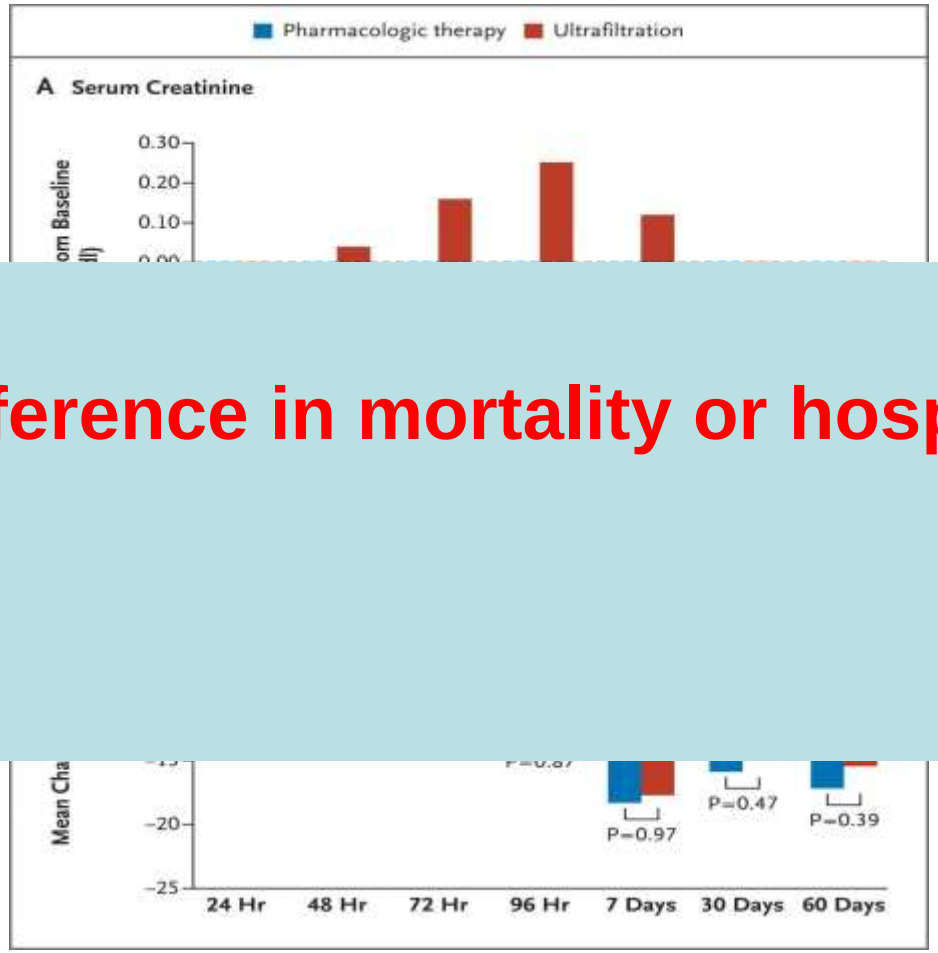
Bart BA et al. N Engl J Med 2012. DOI: 10.1056/NEJMoa1210357

Ultrafiltration or Diuretics in acute cardiorenal failure – CARESS_HF



Bart BA et al. N Engl J Med 2012. DOI: 10.1056/NEJMoa1210357

Ultrafiltration or Diuretics in acute cardiorenal failure – CARESS_HF



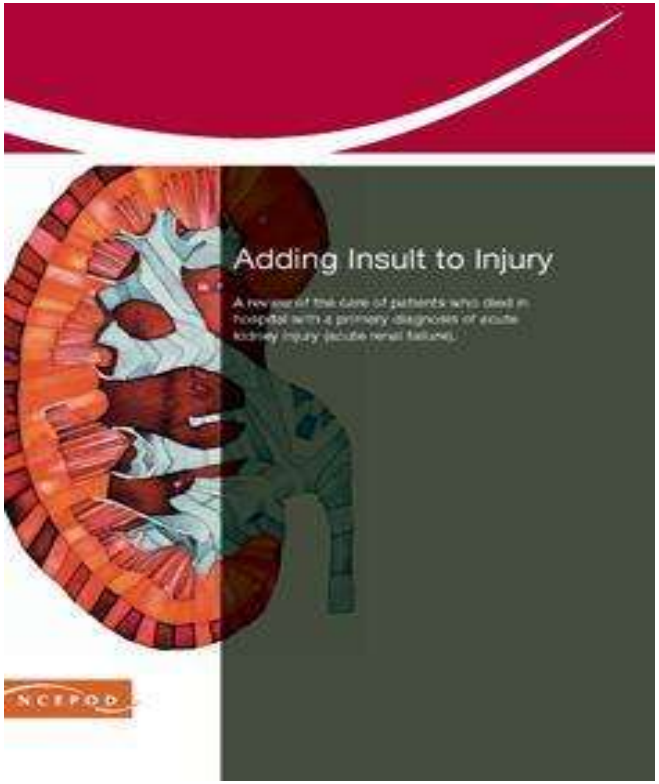
- **No difference in mortality or hospitalisation**

Bart BA et al. N Engl J Med 2012. DOI: 10.1056/NEJMoa1210357

KEY CLINICAL TRIALS

-
- Fluid therapy – what kind and how much?
- RRT – when, what and how much?
- Cardiac surgery – off pump or on pump
- Cardio-Renal failure and contrast nephropathy
- Systems management and AKI

AKI – quality of care issues



Substandard care in 70% of cases in the UK

Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

AKI – HOW TO PRACTICALLY IMPROVE CARE

•

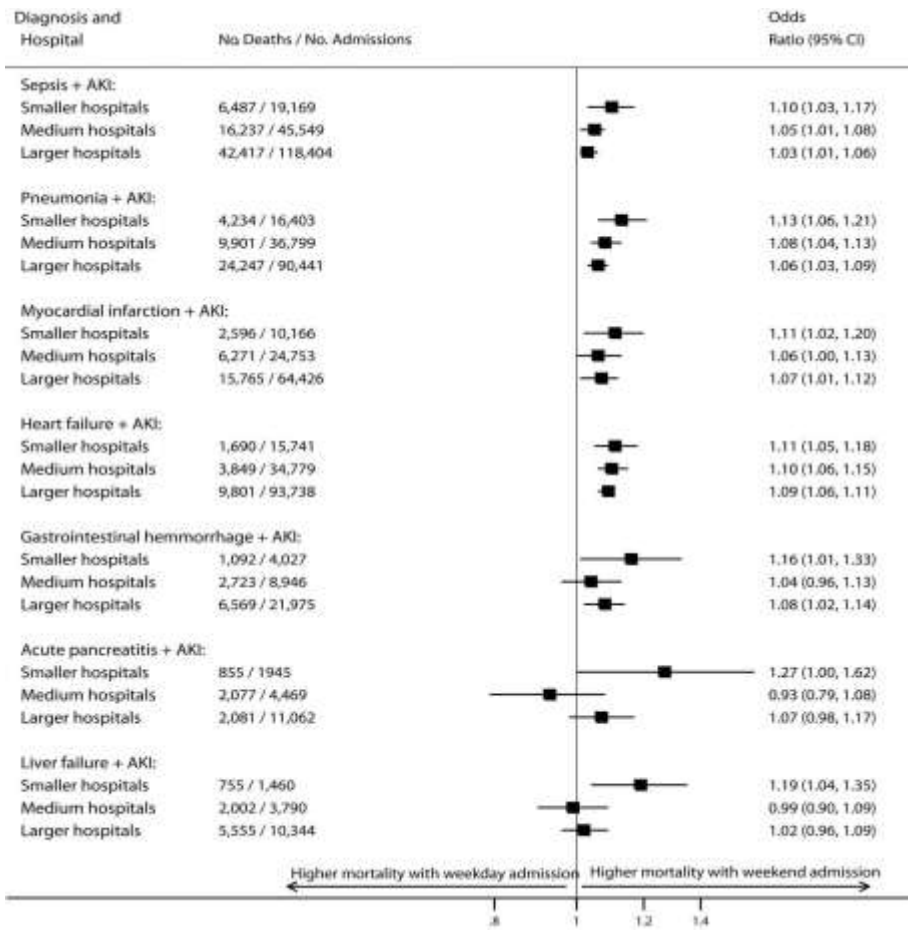
•AKI predominantly occurs in the setting of an ill patient

•AKI is predominantly managed by non-nephrologists

•Improving AKI management needs to target non-nephrologists

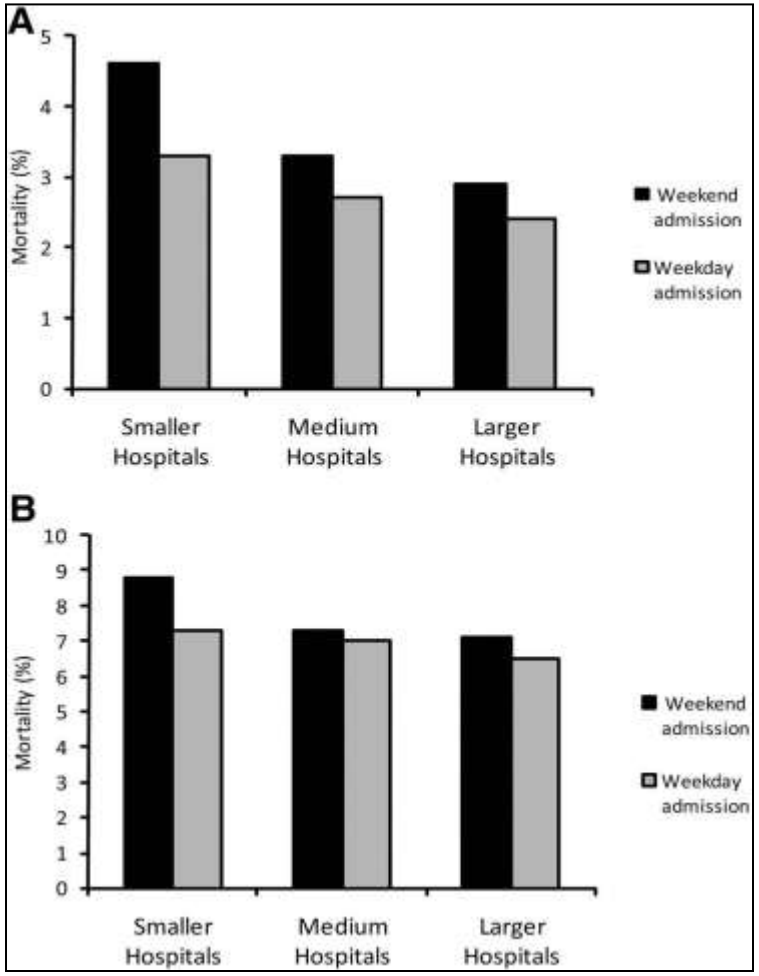
•Use of toolkits, care-bundles to standardise management of the ‘sick’ patient may help

Higher mortality for weekend versus weekday admission across multiple primary acute conditions with AKI as secondary diagnosis



James M T et al. JASN 2010;21:845-851

AKI outcomes by hospital size and weekday



James M T et al. JASN 2010;21:845-851

Electronic Alerts may aid early diagnosis of AKI

Use of electronic results reporting to... [Clin J Am Soc Nephrol. 2012] - PubMed - NCBI - Internet Explorer, optimized for Bing

http://www.ncbi.nl... screenshot windows

File Edit View Favorites Tools Help

Favorites Suggested Sites Free Hotmail Get more Add-ons

Use of electronic results r... Screenshot - Wikipedia, the f...

Page Safety Tools

Find: shot Previous Next Options

Display Settings: Abstract Send to:

Final Version Clin J Am Soc Nephrol

NCBI web applications will no longer support your browser after 1 January 2013. More information here...

Clin J Am Soc Nephrol. 2012 Apr;7(4):533-40. Epub 2012 Feb 23.

Use of electronic results reporting to diagnose and monitor AKI in hospitalized patients.

Selby NM, Crowley L, Fluck RJ, McIntyre CW, Monaghan J, Lawson N, Kolhe NV.

Department of Renal Medicine, Royal Derby Hospital, Derby, UK. nick.selby@nhs.net

Abstract

BACKGROUND AND OBJECTIVES: Many patients with AKI are cared for by non-nephrologists. This can result in variable standards of care that contribute to poor outcomes.

DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS: To improve AKI recognition, a real-time, hospital-wide, electronic reporting system was designed based on current Acute Kidney Injury Network criteria. This system allowed prospective data collection on AKI incidence and outcomes such as mortality rate, length of hospital stay, and renal recovery. The setting was a 1139-bed teaching hospital with a tertiary referral nephrology unit.

RESULTS: An electronic reporting system was successfully introduced into clinical practice (false positive rate, 1.7%; false negative rate, 0.2%). The results showed that there were 3202 AKI episodes in 2619 patients during the 9-month study period (5.4% of hospital admissions). The in-hospital mortality rate was 23.8% and increased with more severe AKI (16.1% for stage 1 AKI versus 36.1% for stage 3) (P<0.001). More severe AKI was associated with longer length of hospital stay for stage 1 (8 days; interquartile range, 13) versus 11 days for stage 3 (interquartile range, 16) (P<0.001) and reduced chance of renal recovery (80.0% in stage 1 AKI versus 58.8% in stage 3) (P<0.001). Utility of the Acute Kidney Injury Network criteria was reduced in those with pre-existing CKD.

CONCLUSIONS: AKI is common in hospitalized patients and is associated with very poor outcomes. The successful implementation of electronic alert systems to aid early recognition of AKI across all acute specialties is one strategy that may help raise standards of care.

PMID: 22362062 [PubMed - indexed for MEDLINE]

Save items

Add to Favorites

Related citations in PubMed

Preexisting chronic kidney disease: a potentia [Clin J Am Soc Nephrol. 2009]

An assessment of the Acute Kidney Injury N [Clin J Am Soc Nephrol. 2011]

Referral patterns and outcomes in noncriti [Clin J Am Soc Nephrol. 2011]

Review Long-term risk of mortality and other adv [Am J Kidney Dis. 2009]

Review Classification and staging of acute kidney i [Nat Rev Nephrol. 2011]

See reviews...

See all...

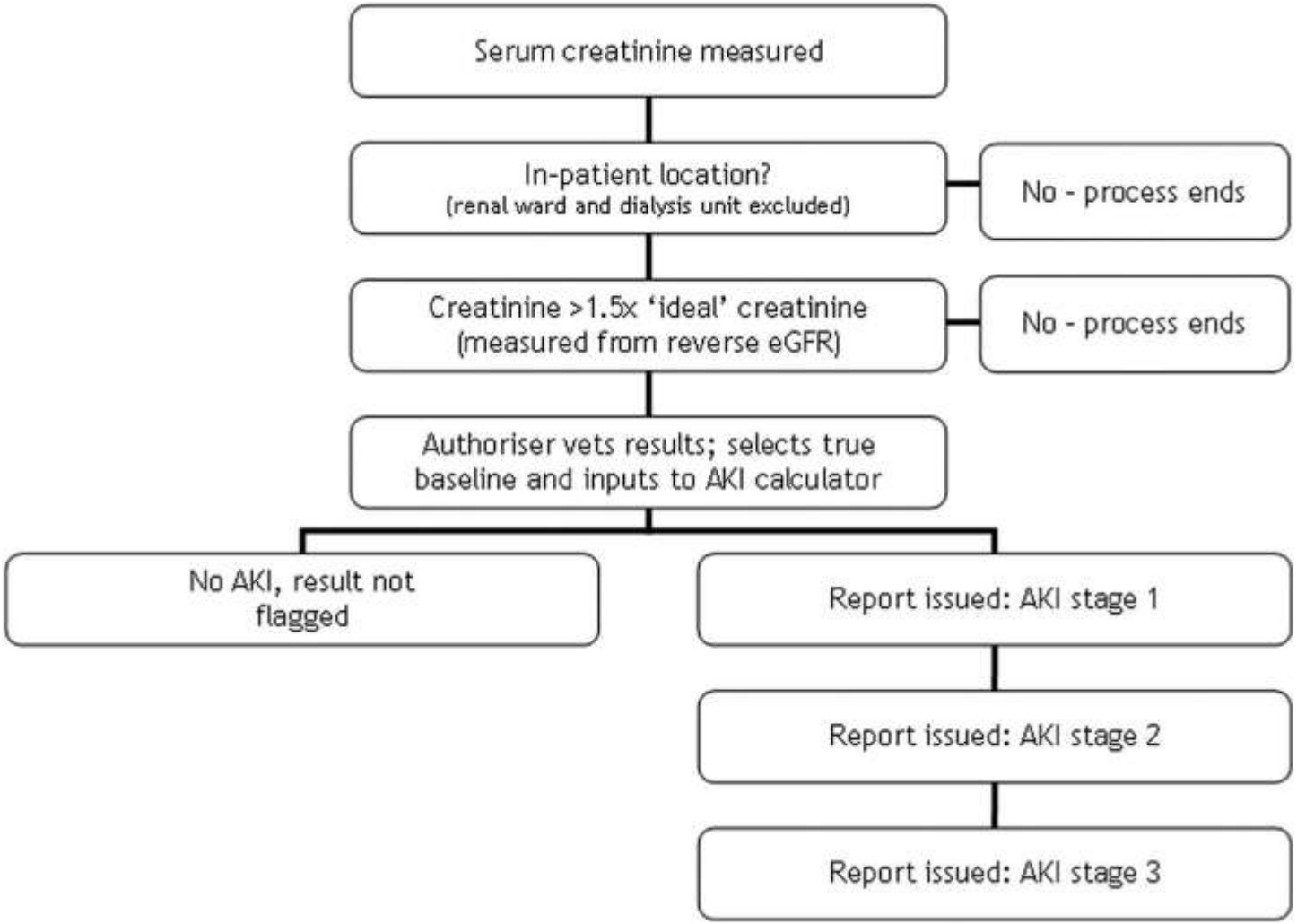
Cited by 1 PubMed Central

Local intranet 100%

Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

Automated AKI reporting – ? An early warning system for AKI



Selby N M et al. CJASN 2012;7:533-540

AKI – UPDATE CONCLUSIONS

-
- AKI is a risk factor for CKD …..
- AKI outcomes are poor
- Saline remains fluid replacement of choice
- Dialysis dose or modality has little impact on outcomes

Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE

AKI – UPDATE CONCLUSIONS

•

•Use of toolkits, care-bundles to standardise management of the ‘sick’ patient may help early diagnosis of AKI…..

•Clinical utility of biomarkers and AKI staging not clear

•There are no treatments that have been shown to improve outcomes in AKI beyond good supportive care

Any Questions

Global Kidney Academy

SHEFFIELD KIDNEY INSTITUTE